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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.

EXAMINER	
ART UNIT	PAPER NUMBER
	5

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/475,072	CADIEUX, ALAIN	
	Examiner	Art Unit	
	Karen Clemens	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☒ The proposed drawing correction filed on *30 December 1999* is: a)☒ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☒ All b)☐ Some * c)☐ None of the CERTIFIED copies of the priority documents have been:

1.☒ received.

2.☐ received in Application No. (Series Code / Serial Number) _____ .

3.☐ received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

15)☒ Notice of References Cited (PTO-892)
16)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18)☐ Interview Summary (PTO-413) Paper No(s). _____ .
19)☐ Notice of Informal Patent Application (PTO-152)
20)☐ Other: .

DETAILED ACTION

The location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1644, Group 1640, Technology Center 1600.

Claims 1-20 are currently pending and are under consideration.

Claim Rejections - 35 U.S.C. § 101

35 U.S.C. § 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

Claims 1-20 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible asserted utility or a well-established utility.

The broadest reasonable interpretation of the claims is the prophylaxis or prevention of the pulmonary disease, asthma. It is noted that "prevent" means to permanently treat any future asthmatic attach. It is assumed that applicant intends to prevent asthma, a bronchospastic disease characterized by airway hyperreactivity or lung inflammatory reaction characterized by increased eosinophilia via administration of CGRP. However, although CGRP has been disclosed in the specification to reduce the intensity of the bronchospasms induced by an asthmatic crisis and to act as an anti-inflammatory agent in the lung (see specification, page 7-9, summary of the invention in particular) the actual prevention of the pulmonary disease, asthma, would require immunological tolerance to the proposed allergen eliciting the inflammatory response prior to the onset of the disease (see Merck Manual, pages 556-568). Therefore, one skilled in the art would not expect a single compound to prevent the disease but rather would prevent the symptoms following the onset of the disease. Therefore the claimed invention is not supported by either a credible asserted utility or a well-established utility.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

A) Claims 1-20 are also rejected under 35 U.S.C. §112, first paragraph. Specifically, since the claimed invention is not supported by a credible or a well-established utility for the same reasons set forth above, one skilled in the art would not know how to use the claimed invention so that it would operate as intended without undue experimentation.

B) Claims 1-20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. The instant claims are drawn to a method for the prophylaxis or treatment of asthma, a bronchospastic disease characterized by airway hyperreactivity or lung inflammatory reaction characterized by increased eosinophilia, using all homologs, analogs, fragments and derivatives of CGRP. However, Applicant has only disclosed the use of CGRP (calcitonin gene related peptide), one natural homolog of CGRP, adrenomedullin, and the linear CGRP analog, [Cys(ACM)^{2,7}] CGRP in clear contrast the number of possible CGRP homologs, analogs, fragments and derivatives encompassed by the instant claims. Consequently the method of prophylaxis or treatment using all homologs, analogs, fragments and derivatives of CGRP is not adequately described. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.*

C) Claims 1-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabled for a method of treatment of asthma, a bronchospastic disease characterized by airway hyperreactivity or lung inflammatory reaction characterized by increased eosinophilia, using CGRP (calcitonin gene related peptide), the natural homolog of CGRP, adrenomedullin and the linear CGRP analog, [Cys(ACM)^{2,7}] CGRP does not reasonably provide enablement for all CGRP homologs, analogs, fragments and derivatives of CGRP. The specification does not enable any person skilled in the art to

which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with the claims.

Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the unpredictability in the art and amount of experimentation required to enable one of skill in the art to practice the claimed invention.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation. The claimed invention encompasses a method for the prophylaxis or treatment of airway hyperreactivity or lung inflammatory reaction characterized by eosinophilia using all homologs, analogs, fragments and derivatives of CGRP. However the specification discloses a method of prophylaxis or treatment using CGRP, the natural homolog of CGRP, adrenomedullin, and the linear CGRP analog, [Cys(ACM)^{2,7}] CGRP (see page 31, lines 13-17 and page 38, lines 24-28) in clear contrast to the large number of CGRP species encompassed by the instant claims.

The specification disclosure describes the claimed CGRP peptides as those which share significant structural and functional homology to CGRP and, as found in the CGRP family, possess the general N-terminal ring structure of 6-7 amino acids involving a disulfide bridge and an amidated C-terminal end (see page 17, lines 3-28). However, the specification provides insufficient guidance on the use of such homologs, analogs, fragments or derivatives of CGRP other than CGRP, adrenomedullin, and the linear CGRP analog, [Cys(ACM)^{2,7}] CGRP, for the prevention or treatment of asthma bronchospasm. The specification disclosure is silent with respect to the specific features necessary for such CGRP homologs, analogs, fragments and derivatives such that they can be used successfully in the method of preventing or treating airway hyperreactivity or lung inflammatory reaction characterized by eosinophilia.

The current state of the art for protein structure/function prediction based on primary amino acid sequence data is currently inadequate given the multifunctional nature of proteins (see Skolnick et al.). Furthermore, It is not routine in the art to screen large numbers of homologs, analogs, fragments and derivatives of CGRP to determine which peptides would possess the functional criteria based on the instant

disclosure. A skilled artisan would require guidance, such as information regarding the amino acid sequences of the homologs, analogs, fragments or derivatives of CGRP required to preserve the biological, structural or functional features of the protein in order to make and use the molecules in a manner reasonably commensurate with the scope of the claims. Therefore, it would take an undue amount of experimentation for one skilled in the art to determine which homologs, analogs, fragments and derivatives of CGRP are encompassed by the instant claims.

In view of the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification, it would take an undue amount of experimentation for one skilled in the art to practice the full scope of the claimed invention.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the Applicant regards as his invention.

Claims 1-20 are rejected under *35 U.S.C. § 112*, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Claims 1-20 are indefinite and ambiguous in reciting "asthma, bronchospastic diseases characterized by airway hyperreactivity or lung inflammatory reaction characterized by increased eosinophilia" in base claim 1. If bronchospastic diseases characterized by airway hyperreactivity or lung inflammatory reaction characterized by increased eosinophilia are the characteristics used to define asthma they should be recited in the dependent claims such as "the method of claim 1, wherein the asthma is characterized by....".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of *35 U.S.C. § 102* that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 1-20 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 5,858,978 as evidenced by the Merck Manual (see pages 556-557).

The 5,858,978 patent teaches a method for the treatment of asthma comprising the administration of CGRP (see column 13, lines 13-19). The '978 patent further teaches the method by administration of a commercially available source of CGRP in a pharmaceutically acceptable carrier administered as an aerosol via the pulmonary route (see column 2, lines 49-50; column 5, line 66-column 6, line 2; column 7, lines 19-49). The '978 patent further teaches the amino-acid composition of human and rat CGRP peptides, and if chemically synthesized, the peptides would inherently reach the 95-98% purity level. The '978 patent teaches that administration of the CGRP peptide is useful in ameliorating abnormal immune response mediated conditions such as asthma. Applicant notes that two major features of asthma include airway hyperreactivity and a massive influx of inflammatory cells, particularly eosinophils in the bronchial walls and lung parenchyma (see specification, page 3 in particular). Furthermore, asthma is known in the art as a bronchospastic disease characterized by airway hyperreactivity and lung inflammatory reaction with an increase in eosinophils (see Merck Manual, pages 556-557 in particular).

Therefore, the reference teachings thus anticipate the claimed invention.

Claim Rejections - 35 U.S.C. § 103

The following is a quotation of *35 U.S.C. § 103* which forms the basis for all obviousness rejections set forth in this Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person subject to an obligation of assignment to the same person.

Claims 1-20 are rejected under *35 U.S.C. § 103(a)* as being unpatentable over Vignery (U.S. Patent No. 5,858,978) in view of Gleich et al. (U.S. Patent No. 5,510,339).

The '978 patent teaches a method for the treatment of asthma comprising the administration of CGRP (see column 13, lines 13-19). The '978 patent further teaches the method by administration of a commercially available source of CGRP in a pharmaceutically acceptable carrier administered as an aerosol via the pulmonary route (see column 2, lines 49-50; column 5, line 66-column 6, line 2; column 7, lines 19-49). The '978 patent further teaches the amino-acid composition of human and rat CGRP peptides suggesting that commercially available sources at the time of the invention, if chemically synthesized, would likely reach the 95-98% purity level. The '978 patent teaches that administration of the CGRP peptide is useful in ameliorating abnormal immune response mediated conditions such as asthma.

However, the '978 patent does not teach a method for the treatment of asthma, in which asthma is specifically described as a bronchospastic disease characterized by airway hyperreactivity or lung inflammatory reaction characterized by increased eosinophilia.

However, the '339 patent teaches that asthma is described as a disease characterized by airway hyperreactivity and lung inflammatory reaction characterized by increased eosinophilia. The '339 patent teaches that eosinophils have long been associated with bronchial asthma and that compounds useful in prevention of eosinophil accumulation and activation would be useful in the therapy for bronchial asthma (see column 1, lines 12-35 and column 4, lines 30-65).

Therefore, it would be been obvious to one having ordinary skill in the art at the time the invention was made to treat asthma, as taught by the '978 patent, which is a bronchospastic disease characterized by airway hyperreactivity or lung inflammatory reaction characterized by increased eosinophilia, as taught by the '339 patent using a highly pure aerosol administered by the pulmonary route as taught by the '978 patent.

One having ordinary skill in the art at the time the invention was made would have been motivated to treat asthma conditions, which are associated with an increased accumulation of eosinophils, as taught by the '339 patent, using CGRP, as taught by the '978 patent because treatment with CGRP is useful in ameliorating abnormal immune response mediated conditions such as asthma as taught by the '978 patent.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Clemens whose telephone number is (703) 308-8365. The examiner can normally be reached Monday through Friday from 8:00 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Karen Clemens, Ph.D.
Patent Examiner
Technology Center 1600
July 31, 2000

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PATENT EXAMINER
7/31/00